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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/419,788	10/18/1999	RAINER FISCHER	0147-0189P	1798

7590 01/29/2002

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EXAMINER
JAMROZ, MARGARET E

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/419,788	Applicant(s) FISCHER ET AL.	
	Examiner Margaret E Jamroz	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 18-42* is/are pending in the application.

4a) Of the above claim(s) *21-28,30-35 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,18-20,29,36 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Notice to comply to Sequence Rules.

DETAILED ACTION

1. Applicant's amendment, filed 2/20/2001 (Paper No. 11), is acknowledged.

Sequence compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is directed specifically to the Brief Description of Figures 2, 14, 21, 23, and 25; and additionally, the primer sequences on pages 68-69 of the specification.

Applicant is reminded to amend the **specification (including the Brief Description of Drawings)** and claims as appropriate to reflect compliance with the Sequence Rules. Specifically, any amino acid sequence longer than 6 residues and any nucleic acid sequence longer than 10 residues must meet the Sequence Rules.

3. Claims 1-14 and 18-42 are pending.

4. Applicant's election with traverse of Group A (claims 1-14, 18-20, 29, 36, and 38-42) with an election of antibody as a binding protein, human T cell receptor transmembrane domain as a membrane localization seuqence as species elections in Paper No. 15 is acknowledged. The traversal is on the ground(s) that all of the claims are drawn to the common essential feature of a binding domain and a membrane localization sequence. Groups B-F have been rejoined with Group A. However, "use" claims (e.g. claim 37) are considered to be method claims; thus they differ from product/composition claims. Therefore, even though the binding domain and membrane localization sequence are common entities within the claims, the inventions as grouped are distinct and independent based on their classification and/or recognized divergent subject matter.

The requirement is still deemed proper and is therefore made FINAL.

Applicant further elects species of antibodies and human T cell membrane domain (Claims 5 and 40). Upon further consideration, the prior art search has been extended to cover other membrane localization sequences as recited in claim 40.

Claims 21-28, 30-35, and 37 (non-elected Groups G-L) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a non-elected invention.

Claims 1-14, 18-20, 29, 36, and 38-42 wherein the fusion protein comprises a binding domain comprising an antibody that specifically recognizes an epitope of a plant pathothen and wherein the membrane localization sequence leads to membrane anchoring are under consideration in the instant application.

5. The abstract of the disclosure is objected to because of the length of the abstract. Correction is required. See MPEP § 608.01(b). Applicant is reminded of the proper language and format for an abstract of the disclosure.

> The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.
>
> The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

6. The drawings are objected to under 37 CFR 1.83(a) because Figure 7 fails to show the c-myc tag as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is directed to page 31 of the specification. All http:// symbols must be removed. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

9. Claims 29 and 36 are objected to as being dependent on non-elected claims 21-26, 28, and 29.

10. Claims 18 and 36 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim, and a claim cannot depend on two sets of different features. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 10, 19-20, and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. The term "RIP" in claim 10, line 2 is a relative term which renders the claim indefinite. The term "RIP" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The examiner suggests amending the claim to recite "ribosomal-inactivating protein (RIP)" so that the abbreviation is defined.

14. The "binding domain as defined in claim 1" recited in claim 19, line 2 has no antecedent basis in base claim 1. Base claim 1 recites a fusion protein.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-14, 18-20, 29, 36, and 38-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of fusion proteins consisting of:
(1) Ab-tag-Tm domain – Figures 2 and 30,
(2) Ab–Tm domain – Figures 3, 7, and 12A,
(3) Carrier-ab-tag – Figure 4,
(4) Ab-Ab-epitope-toxin – Figure 5,
(5) Ab-toxin-tag Figure 13,
(6) Viral coat protein-Ab-tag – Figure 15A, C-D,
(7) Toxin domain-toxin domain-tag – Figure 26B, or
(8) Toxin domain-tag – Figure 26C

wherein the antibody is specific for Tobacco Mosaic Virus coat protein (Fv24 or Fv29), 30K movement protein (Fv30), 54K/183K replicase (Fv54), 3-minute protein (Fv3min), or Cucumber Mosaic Virus movement protein (Fv3a-2).

Applicant is not in possession of any antibodies against **any** other plant viruses, or **any** bacterial, fungal, nematode, insect, or mycoplasma plant pathogens. Applicant is not in possession of any fusion protein comprising at least one binding domain comprising any **antibody** specific for **any** plant pathogen, a membrane localization sequence, and a toxin as recited in claims 2-4 and 9-10; or a pathogenicide comprising the fusion protein of claim 2 (claim 14); any fusion protein wherein the carrier is situated on the C-terminus of the fusion protein (claim 12) or wherein any of the domains comprises a fluorophore (claim 13).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-12, 14, 18-20, and 41-42 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/09398.

The WO document teaches gene constructs comprising **fusion proteins** comprising an **antibody** and **toxin/enzyme** useful against fungi, nematodes, insects, bacteria, and **viruses** (i.e. plant pathogen) which are transformed into plants to make them pathogen-resistant (see the abstract in particular). The invention relates to **recombinant** "chimeric proteins consisting of an antibody or parts there of which is specific for a plague organism or pathogen and a protein which has a toxic effect on said pathogen which has been

constructed by chemically or biochemically linking (i.e. **covalent or non-covalent**) the antibody to the toxin protein or enzyme (see page 2, lines 11-20; page 6, lines 1-5, and claims 1, 4-5, and 7 in particular). The antibody sequences are recombinantly fused directly to a complete enzyme sequence or fused with a flexible linker (see page 5, final paragraph, and page 6, lines 2-6 in particular). Further, "monoclonal antibodies can be raised to almost any epitope or to almost any molecular structure or a pathogen which is vulnerable to ... enzymes" and wherein the toxin/enzyme "can be fused to two or more **antibodies** (or parts thereof) **having different receptors** (see page 2, lines 21-23 and 34-35 in particular). The antibodies can be complete, Fab, F(ab)2, scFv, bivalent scFv (diabody), or any part which binds the target, and are capable of **self-assembly** (see page 5,lines 29-32; and claims 11 and 15 in particular). The "antibodies can be raised to structures of the pathogen which will directly or indirectly lead to resistance of partial resistance when these antibodies are fused to the appropriate toxin or enzyme"; including viral coat proteins ('i.e. see page 3, paragraph 1 in particular). The toxins taught include all proteins that have a toxic effect on pathogens and include enzymes, such as ribosome-inactivating proteins (**RIPs**), **glucanases**, **chitinases**, and **lipase**, which "are able to lyse cells, ... or interfere with ..., replication (i.e. ribosome; see page 4, lines 12 and 24; page 5, lines 1, 19, and 24-28 in particular). The "desired cellular location of the proteins can be achieved using the appropriate targeting sequences. Proteins synthesized without targeting sequences stay in the cytoplasm of the cells, whereas others are directed into the secretory pathway by a signal peptide" (e.g.. **a membrane or cellular targeting sequence**; see page 6, lines 17-27 in particular). Appropriate target organisms/pathogens include fungi, bacteria, nematodes, insects, viruses, and other plant pathogens (see page 6, lines 33-34 in particular). The invention further includes pesticidal compositions containing an immunotoxin with an acceptable **carrier** (see page 8, lines 9-10, and claim 19 in particular). As such, the fusion protein described and claimed is a **pathogenicide**. Although the WO document does not specifically state that the targeting sequence is a "membrane localization sequence and/or motif that leads to membrane anchoring, a membrane is part of a cell, and the WO document encompasses targeting sequence which are directed to several different cellular locations.

Therefore, the WO document anticipates the claimed invention.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 1-12, 14, 18-20, 29, 36, 38, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/09398 in view of U.S. Patent 5,374,548.

The WO document has been discussed supra.

The WO document does not teach fusion proteins comprising binding site that is an antibody and a membrane localization sequence and/or motif that leads to membrane anchoring wherein the membrane localization sequence is proteolytically sensitive (claim 38) or kits (claim 36).

The '548 patent teaches **fusion proteins** utilizing a **GPI** signal domain (i.e. **membrane localization sequence**) to enable the fusion protein to target biological activity to cell-membrane surfaces, and wherein the GPI is fused to immunoglobulins (e.g. antibodies) or enzymes (e.g. RIPs) utilizing recombinant technology (see column 3, lines 30-68; and column 4, first paragraph in particular). The carboxyl terminal domain specifics a glycophospholipid membrane anchor which can be conjugated to antigens from infectious organisms, allergens, immunoglobulins, enzymes and receptors. The GPI anchor specifies a processing event in the cell that results in cleavage and removal of the GPI signal domain. Therefore, the GPI signal domain is proteolytically removed (e.g. **proteolytically sensitive**) and replaced with a hydrophobic glycolipid (GPI) that acts as a membrane anchor (see column 3, paragraph 4 in particular). The '548 patent further teaches **kits** encompassing the fused polypeptide (see column 9, paragraph 4 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the recombinant, generic GPI membrane localization sequence taught by the '548 patent in the in the recombinant fusion protein directed against a viral plant pathogen taught by the WO document. Furthermore, it would have been obvious that kits could be made comprising the fusion protein for application to plants.

One of ordinary skill in the art would have been motivated to do this because the membrane localization sequences both direct the fusion protein to anchor to a specific cellular location, such as a membrane. The fusion proteins taught by all four patents clearly indicate that one of ordinary skill in the art would have a reasonable expectation of success in creating the claimed invention utilizing the recombinant techniques described.

21. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/09398 in view of U.S. Patent 5,374,548 as applied to claims 1-12, 14, 18-20, 29, 38, and 40-42 above, and further in view of U.S. Patent 5,698,679.

The WO document and '540 patent have been discussed supra.
The combined teachings of the WO document and '540 patent do not teach a fusion protein wherein the membrane localization sequence is a member of the immunoglobulin superfamily.

The '679 patent teaches an immunoglobulin fusion protein comprising a **membrane localization sequence** wherein an immunoglobulin C_H region is useful in the production of a membrane bound immunoglobulin fusion protein (see column 10, lines 37-47 in particular). "Preferably, the C_H region contains at least one **immunoglobulin transmembrane domain**" (see column 10, lines 52-54 in particular). The '679 patent further teaches that a membrane bound fusion protein is "particular advantageous because the fusion proteins can be co-delivered with other useful reagents, such as **toxins** and **enzymes** (see column 10, lines 54-58 in particular). Finally, the '679 patent teaches recombinant techniques and nucleic acid sequences for the fusion proteins (see column 13, paragraph 3 in particular).

It would be obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunoglobulin superfamily membrane localization sequence taught by the '679 patent and the GPI anchor taught by the '548 patent for the fusion protein taught by the WO patent because the both the GPI anchor and the immunoglobulin superfamily membrane localization sequences allow for localization of the protein to a particular cellular/membrane location.

One of ordinary skill in the art would have been motivated to do this because the membrane bound fusion protein is "particular advantageous because the fusion proteins can be co-delivered with other useful reagents, such as toxins and enzymes as taught by the '679 patent.

22. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/09398 in view of U.S. Patent 5,374,548 as applied to claims 1-12, 14, 18-20, 29, 38, and 40-42 above, and further in view of U.S. Patent 5,876,950.

The WO document and the '548 patent have been discussed supra.
The combined reference teachings do not teach fusion proteins comprising a fluorophor (claim 13).

The '950 patent teaches compositions comprising recombinant binding proteins labeled with a detectable marker, such as a **fluorophor**, and methods for conjugation or linkage of the antibody to the **detectable marker**. The '950 patent further teaches compositions comprising monoclonal **antibodies** or recombinant binding proteins **conjugated or linked** to a therapeutic agent, such as a **toxin**, and pharmaceutical compositions comprising an acceptable **carrier** (see column 12 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the fluorophor taught by the '950 patent in the fusion protein taught by the WO document and the '548 patent.

One of ordinary skill in the art would have been motivated to do this because the fluorophor allowed for detection of the fusion protein as taught by the '950 patent.

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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January 22, 2002

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